Study of Red Piper Betle Leaf (*Piper crocatum* Ruiz & Pav.)
Ethanolic Extract Effect on Gastric Mucosa

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Abstract

The present study was designed to clarify the effects of an ethanol extract of red piper betle extract in the Wistar strain of female rats after long-term use. The rats were classified into normal control, negative control and test group that given the extract in a dose of 500 mg/kg body weight. The red piper betle extract was given orally to Wistar rats for a period of 90 days. Then gastric mucosal conditions were examined macroscopically and observed under a magnifying glass to see if there are ulcers, the number and width of the ulcer. The calculation was done using scoring method, hereinafter determined the ulcer index. From the observation result, showed that gastric mucosal condition based on scores did not show any ulcers, either in the control group or the test group. The result suggest that the ethanol extract of red betel leaf does not cause damage to gastric mucosa after long term in use.

Keywords: Piper crocatum, extract, gastric, mucosa, ulcer, effect.

Introduction

One of the potential medicinal plants that are potent to cure various type of disease, especially infectious diseases, are Red betel leaves (*Piper crocatum*) [1]. Its ability as a natural medicine, has been widely proven through several studies. The results of some studies showed that the ethanol extract of red piper betel leaves has antibacterial and antifungal activity [2,3]. The extract has also been studied to be a natural remedy for anti-inflammatory, wounds, antioxidants and used to cure various diseases such as hepatitis, diabetes, kidney failure, stroke, hypertension, and etc [4,5,6,7]. The secondary metabolite content contained in the extract plays an important role in producing various pharmacological effects. As reported in another study, the red piper betel leaves extract have several metabolites, such as flavonoids, polyphenolics, steroids, quinones, and saponins [8]. Besides that, the red piper betel leaves have a more fragrant aroma than the green betel leaves. Owned fragrant aromas of red betel are one of the advantages that can be used as a natural fragrance in pharmaceutical preparations [2].

Due to its widespread use in the field of health, people often use this red piper betel leaf as a preventative medicine every day. But every new chemical must be examined for its toxic properties before its wide-ranging use. Because there are some reports about the side effect of herbal product consumption [9]. Extracts consumed in the long term should be believed to be safe for consumers. One of the observed toxicity parameters was the effect of extract on gastric mucosa. The gastric ulcer therapy
faces a major drawback in modern days due to the unpredictable side effects of the long-term uses of commercially available drugs and affects 5% of the global population [10].

**Materials and Methods**

**Plant Materials**
The leaves of red Piper betel (*Piper crocatum* Ruiz and Pav.) were obtained from Bogor, Indonesia and determined in Plant Taxonomy Laboratory of Biology Major, Faculty of Mathematics and Natural Science Padjadjaran University, Bandung, Indonesia.

**Animal**
Female Wistar rats were purchased from Laboratory Animal in School of Life Sciences and Technology, Bandung Institute of Technology, Bandung, Indonesia. The rats were aged of 8-12 weeks and weighing 170 –185 g.

**Methods**

**Extraction**
The simplicia powder of red piper betel leaves were extracted by maceration for 3 x 24 h using 70% ethanol as a solvent. The macerates was collected every 24 h and evaporated in rotary evaporator to obtained concentrated extracts with constant weight [1].

**Phytochemical screening**
The phytochemical tests were conducted to detect the presence of polyphenols, tannins, alkaloids, quinones, saponins, flavonoids, monoterpenoid, steroids, triterpenoid, and sesquiterpenoid, described by Fansworth [11]. The precipitate formation and color intensity after the addition of certain reagents, were observed.

**Animal Treatment**
The rats were acclimatized to laboratory conditions for 7 d prior to the experiments. The rats were kept at room temperature of 22° ± 3° C with a 12 h light and dark cycle. During acclimatization, the rats were fed and drank using pellet and water according to laboratory standards. Wistar female Wistar strains were divided into 2 groups, the control group and the test group. The control group was given a 10% PGA suspension. The test group was given ethanol extract of red betel leaf dose 500 mg / kg BW in PGA 10% suspension. Administration of the test preparation was performed daily for 90 days, administered orally using syringe and oral sonde volume of 2 mL/200 g of rat [1].

**Examination of the Animal Gastric Mucosal Ulcer Test Index**
The condition of the gastric mucosa was examined macroscopically and observed under a magnifying glass to see if there was an ulcer, as well as to know the number and width of the ulcer. The calculation was done by the next scoring method to determine ulcer index, could be seen in table 1-2.

**Table 1: Scoring based on ulcer number**

<table>
<thead>
<tr>
<th>Mucosal condition</th>
<th>Scores</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>1</td>
</tr>
<tr>
<td>The bleeding spot</td>
<td>2</td>
</tr>
<tr>
<td>1-3 pieces in Number of ulcers</td>
<td>3</td>
</tr>
<tr>
<td>4-6 pieces in Number of ulcers</td>
<td>4</td>
</tr>
<tr>
<td>7-9 pieces in Number of ulcers</td>
<td>5</td>
</tr>
<tr>
<td>Perforation</td>
<td>6</td>
</tr>
</tbody>
</table>

**Table 2: Scoring based on ulcer diameter**
Results and Discussion

Phytochemical Screening Results
Phytochemical screening was performed to determine the presence of a secondary metabolite group contained in simplicia and extracts. Based on the results of phytochemical screening of simplicia and extract from red piper betle leaves, it contained of several secondary metabolites such as alkaloids, flavonoids, polyphenols, quinones, and saponins.

Result of Examination of Ulcer Index
The observation of gastric mucosal condition based on scores did not show any ulcers in rat stomach, either in the control group or the test group. These results indicate that the extract of red betel leaf ethanol does not cause damage to the stomach organs. Observation of gastric mucosal condition based on scores was performed in table 3.

Table 3: Results of Ulcer Index Calculation

<table>
<thead>
<tr>
<th>Group</th>
<th>Percent of Animals Having Ulcers</th>
<th>Ulcer Index</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>0</td>
<td>2.00</td>
</tr>
</tbody>
</table>

Peptic ulcers occur upon the disruption of the normal equilibrium between aggressive factors, such as acid and pepsin, and defensive mechanisms, such as mucus production, bicarbonate, mucosal turnover, and blood supply (mucosal barrier) [12]. The gastroprotective effect of the extract could be due to its antioxidant properties [13]. Many bioactive metabolites such as polyphenol, flavonoid and tannin are reported having antioxidant, anti-inflammatory, ulcer protective and healing effects [14, 15]. Previous studies have shown that antioxidants may be connected to antiulcer activity through gastroprotection [15,16]. Moreover, it is evident that red piper betel extract contains certain constituent(s) that have toxic effects.

Conclusion
The result suggested that the ethanol extract of red betel leaf does not cause damage to gastric mucosa after long term in use.

References
2. Kusuma SAF, Hendriani R, Genta A, “Antimicrobial spectrum of red piper betel leaf extract (Piper crocatum Ruiz & Pav) as natural antiseptics against
